REMARKS

Applicants now respond to the Office Action mailed May 27, 2005. Reconsideration of this application and reexamination of the claims in view of the remarks herein are respectfully requested.

The Office objected to the specification because the first paragraph referred to Application No. 08/466,698, filed June 6, 1995, as pending, though in fact the application has now become abandoned. Applicants have corrected the information regarding the status of the '698 application appearing in the first paragraph to reflect that the '698 application is abandoned. Accordingly this objection to the specification may be withdrawn.

Claims 14-52 are pending and stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Specifically, the Office contends that "[t]he clams are vague and indefinite in the recitation of can not spread 'substantially' within infected cells and can not spread 'substantially' from infected to uninfected cells." According to the Office, "[o]ne of skill in the art would be unable to determine the metes and bounds of the claimed invention. For instance, what level of spreading is permitted to qualify as not substantial? Similarly, at what level does it exceed the threshold to be deemed substantial?" Applicants respectfully traverse, and submit that the claims are definite.

"The essential inquiry pertaining to [the requirement for definiteness] is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity." (MPEP § 2173.02.) A claim satisfies this standard if a person of ordinary skill in the art, as of the filing date of the application, would understand the bounds of the claim when read in light of the specification. *See*

Howmedica Osteonics Corp. v. Tranquil Prospects, Ltd., 401 F.3d 1367, 1371, 74 U.S.P.Q.2d 1680, 1683 (Fed. Cir. 2005). The pending claims meet this standard.

In construing the term "substantial" in patent claims, the Federal Circuit has stated that "[t]he term 'substantial' is a meaningful modifier implying 'approximate,' rather than 'perfect'." *Playtex Prods., Inc. v. Procter & Gamble Co.*, 400 F.3d 901, 907, 73 U.S.P.Q. 2010 (Fed. Cir. 2005). This is consistent with how the term is used in the specification and with how one of skill in the art would have understood it in the claims, as of the July 18, 1988, priority date of the instant application.

The application states:

> This invention relates to a method of modifying the genome of an entero-invasive wild strain of Shigella so that the strain cannot substantially invade cells and tissues of an infected host and cannot spread substantially within infected cells and between infected and non-infected cells of the host and cannot produce toxins which will kill substantial numbers of the hosts' cells.

(Page 1, lines 4-11.)

The application goes on to state that "This invention particularly relates to such a modified strain of Shigella which can be used to immunize a host against the wild strain of Shigella. (Page 1, lines 11-13.) (See also page 4, lines 29-31.) Later, the application discusses formulating vaccines with the strains. (Page 6.) Thus, one of skill in the art, reading the application, would have understood that the claimed strains are to be used in immunogenic compositions to immunize a host against an infection by a wild strain of *Shigella*. This is also made clear by the claims themselves, which recite, *e.g.*, "A method for modifying a wild strain of an enteroinvasive *Shigella* to produce a modified strain of *Shigella* . . . for use in making a vaccine against the wild strain of *Shigella*." (claim 14).

The Declaration of Stewart Thomas Cole, Ph.D. ("Cole Declaration") was attached to the Supplemental Preliminary Amendment, filed August 17, 2004. According to Dr. Cole "The '698 application describes modified strains of *Shigella* that can be used to make a vaccine against a wild strain of *Shigella*." (Cole Declaration at ¶ 12.) Based on this disclosure, Dr. Cole concluded that

> Although the '698 application does not use the term, this type of strain was known as of July 15, 1988, as it is today, as a "live attenuated strain". For a live attenuated strain to function effectively as a vaccine, **the strain must be modified by mutation of one or more genes to eliminate its pathogenicity, but not the ability of the strain to elicit a protective immune response**. Such strains were known as of July 15, 1988. For example, the "International Dictionary of Medicine and Biology", published in 1986, defined an "attenuated vaccine" at page 3083 as "A live bacterial or viral vaccine, carrying mutations that eliminate its pathogenicity but not its ability to elicit a protective immune response."

(Cole Declaration at ¶ 12, emphasis added.)

Dr. Cole then explained that

> As of July 15, 1988, it was known that making a live attenuated *Shigella* strain would require modifying a wild *Shigella* strain by mutating one or more genes required for pathogenicity of the wild strain, to create a modified strain that will invade and multiply in a host, but, unlike the corresponding wild strain, will not cause a disease pathology.

(Cole Declaration at ¶ 13.)

As a result of this knowledge in the art, Dr. Cole explained that,

> It was appreciated that, while attenuation of the live attenuated strain is critical to render the strain non pathogenic, it is imperative that the strain retain some ability to invade, multiply, and spread within an inoculated host, so that the strain elicits a significant enough immune response to confer immunity to the wild strain to the host.

(Cole Declaration at ¶ 13.)

Throughout the remainder of his Declaration Dr. Cole then applied this understanding to the claim language, stating that he understood the claim language to mean that "the ability of the [claimed] strain[s] to spread within infected host cells, and from infected to uninfected host cells, is substantially reduced." (*E.g.*, Cole Declaration at ¶ 14.) He made clear that "substantially reduced" does not mean completely reduced, noting that "the ability of the strain to spread within infected host cells, and from infected to uninfected host cells, is clearly not abolished. If it were, the modified strain would not be useful to make a vaccine against the wild strain of *Shigella*." (*E.g.*, Cole Declaration at ¶ 14.)

Thus, the Cole Declaration construed the language in the claims, that the modified strain of *Shigella* "can not spread substantially within infected cells of a host and can not spread substantially from infected to uninfected cells of the host," as defining definite upper and lower limits to the degree to which the claimed strains can spread within infected cells of a host and from infected to uninfected cells of the host.

The upper limit to the strains' ability to spread is defined by the fact that the strain may be used as a vaccine. Thus, the strain must be modified by mutation to eliminate its pathogenicity. The claimed methods provide such a modification.

The lower limit to the strains' ability to spread is also defined by the fact that the strain may be used as a vaccine. Thus, the strain must be modified by mutation in a manner that preserves the ability of the strain to elicit a protective immune response. The claimed methods provide such a modification.

Applicants submit that one of skill in the art, as of the July 15, 1988, effective filing date of this application, would have understood, as Dr. Cole explains, the bounds of the claims when read in light of the specification. Therefore, the claims are definite and the rejection under 35 U.S.C. § 112, first paragraph should be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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By: 

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